Detailed Action

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/28/08 has been entered.

Claims 1, 4-8, 11, 14, 19-21, 24, 28-30, and 35-37 are pending.

Claims 1, 14, 24, 28, and 35-37 have been amended by Applicant.

Claims 1, 4-8, 11, 14, 19-21, 24, 28-30, and 35-37 are currently under consideration.

The following Office Action contains a new rejection based on a reference found in the IDS filed 9/8/08.

Rejections Withdrawn

The rejection of claims 14, 20, 24, 29, 36 and 37 under 35 U.S.C. 103(a), as being unpatentable over Loktionov et al (Clinical Cancer Research, February 1998, 4(2): 337-342) in view of Hromadnikova et al (BMC Pregnancy and Childbirth, 5/28/02, 2(4):1-5), is withdrawn.

Response to Arguments

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14, 19-21, 24, 28-30, 36, and 37 remain rejected under 35 U.S.C. 112, first paragraph, for the reasons stated in the Office Action of 8/23/07, the reasons stated in the Office Action of 4/28/08, and for the reasons set-forth below.

The specification, while being enabling for a method for diagnosing colorectal cancer in a patient comprising the steps of measuring a quantitative amount of genome equivalents of patient genomic DNA in a stool sample comprising shed cells or cell debris, wherein the quantitative amount of genome equivalents is measured by measuring an amount of fragments of less than 200bp; and if the amount of genome equivalents is above a predetermined threshold amount of genome equivalents, determining whether there is a statically significantly larger amount of nucleic acids greater than 200bp in length in said patient sample as compared to the amount of nucleic acids greater than 200bp in length in stool of a healthy subject wherein the presence of said significantly larger amount indicates the patient has colorectal cancer, **the specification does not reasonably provide enablement for** methods for diagnosing colorectal cancer in a patient comprising the steps of measuring a quantitative amount of genome equivalents of patient genomic DNA in a stool sample comprising shed cells or cell debris, wherein the quantitative amount of genome equivalents is measured by measuring an amount of fragments of less than 200bp; and

if the amount of genome equivalents is above a predetermined threshold amount of genome equivalents, performing an additional assay selected from the group of a DNA integrity assay, an assay detecting just any mutation, just any LOH assay, just any assay detecting just any type of expression, and a FISH assay detecting just any biomarker and wherein just any "positive" result from said any additional assay indicates said patient has cancer, has precancer, or has abnormal proliferating colorectal cancer cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *Ex parte* Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The instant claims are broadly drawn to methods for diagnosing colorectal cancer in a patient comprising the steps of measuring a quantitative amount of genome equivalents of patient genomic DNA in a stool sample comprising shed cells or cell debris, wherein the quantitative amount of genome equivalents is measured by measuring an amount of fragments of less than 200bp; and if the amount of genome equivalents is above a predetermined threshold amount of genome equivalents,

performing an additional assay selected from the group of a DNA integrity assay, an assay detecting just any mutation, just any LOH assay, just any assay detecting just any type of expression, and a FISH assay detecting just any biomarker and wherein just any "positive" result from said any additional assay indicates said patient has cancer, has precancer, or has abnormal proliferating colorectal cancer cells.

The specification teaches a method for diagnosing colorectal cancer in a patient comprising the steps of measuring a quantitative amount of genome equivalents of patient genomic DNA in a stool sample comprising shed cells or cell debris, wherein the quantitative amount of genome equivalents is measured by measuring an amount of fragments of less than 200bp; and if the amount of genome equivalents is above a predetermined threshold amount of genome equivalents, determining whether there is a statically significantly larger amount of nucleic acids greater than 200bp in length in said patient sample as compared to the amount of nucleic acids greater than 200bp in length in stool of a healthy subject wherein the presence of said significantly larger amount indicates the patient has colorectal cancer (see pages 12-16, in particular).

The state of the prior art dictates that if a particular assay is to predictably determine the presence of a particular disease state, such as a particular cancer, a particular result from said assay must be identified in some way with said particular disease state. There must be some pattern that would allow the marker to predictably used in a diagnostic manner with success. For example, Tockman et al (Cancer Res., 1992, 52:2711s-2718s) teach considerations necessary in bringing a cancer biomarker (intermediate end point marker) to successful application. Tockman et al teaches that

prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials (see abstract). Early stage markers of carcinogenesis have clear biological plausibility as markers of preclinical cancer and if validated (emphasis added) can be used for population screening (p. 2713s, col 1). The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome. Therefore, absent evidence of results from a particular assay correlating to a particular diseased state, one of skill in the art would not predict that a “positive" result from said assay detects said particular diseased state without undue experimentation.

The level of unpredictability that just any “positive” result from just any assay encompassed by the instant claims would detect just any cancer is quite high. Since neither the specification nor the prior art provide evidence of a universal association between every positive result of every assay and colorectal cancer, a practitioner wishing to practice the claimed invention would be required to provide extensive experimentation to demonstrate such an association. Such experimentation would in itself be inventive.

One cannot extrapolate the teachings of the specification to the scope of the claims because the claims are broadly drawn to methods for diagnosing colorectal cancer in a patient comprising the steps of measuring a quantitative amount of genome equivalents of patient genomic DNA in a stool sample comprising shed cells or cell

debris, wherein the quantitative amount of genome equivalents is measured by measuring an amount of fragments of less than 200bp; and if the amount of genome equivalents is above a predetermined threshold amount of genome equivalents, performing an additional assay selected from the group of a DNA integrity assay, an assay detecting just any mutation, just any LOH assay, just any assay detecting just any type of expression, and a FISH assay detecting just any biomarker and wherein just any "positive” result from said any additional assay indicates said patient has cancer, has precancer, or has abnormal proliferating colorectal cancer cells, and Applicant has not enabled said methods because it has not been shown that just any “positive” result from just any assay selected from the group of a DNA integrity assay, an assay detecting just any mutation, just any LOH assay, just any assay detecting just any type of expression, and a FISH assay detecting just any biomarker indicates a patient has cancer, has precancer, or has abnormal proliferating colorectal cancer cells.

In view of the teachings above and the lack of guidance, workable examples and or exemplification in the specification, it would require undue experimentation by one of skill in the art to determine with any predictability, that the method would function as broadly claimed.

In the Reply of 8/28/08, Applicant amended claims 14 and 24 to recite that the “at least one additional assay” is selected from the group consisting of a DNA integrity assay, mutation detection, enumerated loss of heterozygosity (LOH), expression assays, and fluorescent in situ hybridization (FISH). Applicant indicates these amendments would obviate this rejection.

The amendments to the claims and the arguments found in the Reply of 8/28/08 have been carefully considered, but are not deemed persuasive. In regards the amendments, one of skill in the art would not predict that the methods would function as broadly claimed for the reasons stated above. Particularly, one would not predict that just any “positive” result from just any assay selected from the group of a DNA integrity assay, an assay detecting just any mutation, just any LOH assay, just any assay detecting just any type of expression, and a FISH assay detecting just any biomarker indicates a patient has cancer, has precancer, or has abnormal proliferating colorectal cancer cells. Without stating what result is a "positive" result, every result encompasses a positive result. Further, assays of the claimed methods encompass detecting biomarkers (mutations, expression, etc) that are not indicative of cancer, precancer, or abnormal proliferating colorectal cancer cells.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4, 7, 11, and 35 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Loktionov et al (Clinical Cancer Research, February 1998, 4(2): 337-342) in view of Hromadnikova et al (BMC Pregnancy and Childbirth, 5/28/02, 2(4):1-5)

for the reasons stated in the Office Action of 8/23/07, the reasons stated in the Office Action of 4/28/08, and for the reasons set-forth below.

The claims comprise methods of detecting colorectal cancer comprising detecting genomic DNA in stool samples comprising shed cells and shed cellular debris comprising measuring an amount of amplified nucleic acid fragments having length of 200 bp or less.

Loktionov et al teaches a method for diagnosing and screening a patient for the presence of colorectal cancer comprising using PCR to detect an amount of amplified 113 bp fragments of patient DNA in a stool sample to confirm DNA quality in order to identify a patient as a candidate for additional cancer testing if the amount is above a predetermined threshold amount, which would indicate a positive screen, before additional steps of diagnostic tests/examinations on the patient's stool sample for detecting the presence of colorectal cancer are performed (see Figure 1 and page 338 , in particular). As evidenced by Lapidus et al (US 6,143,529; 11/7/00), stool samples comprise shed cells and cellular debris (see lines 52-57 of column 4, in particular). Loktionov et al further teaches said additional steps include an assay using 260/280 nm absorbance to detect the presence of colorectal cancer by detecting a quantitative amount of genomic DNA in a stool sample by determining a 260:280 ratio (see Table 2, Figure 2, and the paragraph spanning pages 340-340, in particular). Loktionov et al further teaches, and one of skill in the art would recognize, that methods of screening for colorectal cancer are methods of screening for the presence of abnormal proliferating colorectal cancer cells (see page 340, in particular).

Loktionov et al does not specifically teach the amounts of 113 bp fragments of patient DNA expressed in terms of “genome equivalents” or that the PCR method is “quantitative PCR”. However, these deficiencies are made up in the teachings of Hromadnikova et al.

Hromadnikova et al teaches a quantitative PCR method of comparing amounts of DNA between samples comprising expressing amounts of DNA in terms of “genome equivalents” (page 2 right column, in particular).

One of ordinary skill in the art at the time the invention was made would have been motivated to perform the methods taught by Loktionov et al using quantitative PCR, and express the amplified 113 bp fragments of patient DNA in terms of genomic equivalents because using highly quantitative assays and expressing amounts of DNA in terms of genomic equivalents effectively normalizes data between multiple samples and assays and Loktionov et al teaches data from multiple samples or assays is to be compared before additional steps of diagnostic tests/examinations on the patient’s stool sample for detecting the presence of colorectal cancer are performed (see Figure 1 and page 338 , in particular). One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for performing quantitative PCR and expressing the measured amounts of DNA in the method taught by Loktionov in terms of genomic equivalents because Hromadnikova et al teaches a quantitative PCR method and methods of expressing amounts of DNA as “genome equivalents” (page 2 right column, in particular). Therefore, the invention as a whole would have

been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

In the Reply of 8/28/08, Applicant argues that Loktionov et al does not disclose measuring genomic DNA from a stool sample comprising shed cells and cellular debris, but teaches measuring an amount of DNA extracted from whole cells isolated from a stool sample. Applicant further argues that the present invention is determining a quantitative amount of patient genomic DNA in a stool sample from both the DNA contained within intact exfoliated cells and substantially degraded DNA contained within shed cellular debris and that Loktionov et al only teaches a method of determining an amount of DNA in a subpopulation of the DNA that is present in a stool sample. Applicant further argues that Loktionov et al does not isolate shed cellular debris that is naturally present in a stool sample and Loktionov's method cannot be used for determining a quantitative amount of genome equivalents of patient genomic DNA in a stool sample comprising shed cells and shed cellular debris. Applicant further argues that Loktionov does not teach or suggest that detection of a 113 bp fragment was used to identify a patient as a candidate for additional testing. Applicant further argues that Hromadnikova does not teach or suggest determining a quantitative amount of genome equivalents of patient genomic DNA in a stools sample comprising shed cells and cellular debris. Applicant further states that it was unexpected that measuring nucleic acid fragments of length 200bp or less could distinguish healthy patients from those that should undergo additional cancer testing and that said fragments having length of 200bp or less surprisingly provides an accurate measurement because it is indicative of

the total amount of DNA that is present in a stool sample of both healthy individuals and cancer patients.

The amendments to the claims and the arguments found in the Reply of 8/28/08 have been carefully considered, but are not deemed persuasive. In regards to the argument that Loktionov et al teaches measuring an amount of DNA extracted from whole cells isolated from a stool sample and does not teach measuring genomic DNA from a stool sample comprising shed cells and cellular debris, the instant claims are not limited to methods wherein measured amounts of amplified nucleic acid fragments are required to be measured from an amplified product produced by both shed cells and shed cellular debris. Rather, the instant claims are drawn to a method of determining “a” quantitative amount of genome equivalents of patient genomic DNA in a stool sample comprising shed cells and shed cellular debris, wherein the quantitative amount of genome equivalents is determined by measuring “an” amount of amplified nucleic acid fragments. The claims do not provide any limitation as to where or how said amplified nucleic acid fragments are to be obtained from the sample or any limitation requiring determining “the total” amount of DNA in a stool sample comprising shed cells and shed cellular debris.

In regards to the argument that the present invention is determining a quantitative amount of patient genomic DNA in a stool sample from both the DNA contained within intact exfoliated cells and substantially degraded DNA contained within shed cellular debris and that Loktionov et al only teaches a method of determining an amount of DNA in a subpopulation of the DNA that is present in a stool sample,

Applicant is arguing limitations not recited in the claims. The claims do not require one to determine the total amount of DNA in a stool sample from both the DNA in a stool sample from both the DNA contained within intact exfoliated cells and substantially degraded DNA contained within shed cellular debris; rather, the claims are drawn to a method of determining “a” quantitative amount of genome equivalents of patient genomic DNA in a stool sample comprising shed cells and shed cellular debris, wherein the quantitative amount of genome equivalents is determined by measuring “an” amount of amplified nucleic acid fragments. The claims do not provide any limitation as to where or how said amplified nucleic acid fragments are to be obtained from the sample or any limitation requiring determining “the total” amount of DNA in a stool sample comprising shed cells and shed cellular debris.

In regards to the argument that Loktionov et al does not isolate shed cellular debris that is naturally present in a stool sample, Applicant is arguing limitations not recited in the claims. The claims do not require one to isolate shed cellular debris.

In regards to the argument that Loktionov's method cannot be used for determining a quantitative amount of genome equivalents of patient genomic DNA in a stool sample comprising shed cells and shed cellular debris, Loktionov et al teaches a method comprising determining an amount of amplified 113 bp fragments of patient genomic DNA in a stool sample. As evidenced by Lapidus et al (US 6,143,529; 11/7/00), stool samples comprise shed cells and cellular debris (see lines 52-57 of column 4, in particular). Further, while Loktionov et al determines said amount of amplified 113 bp fragments of patient genomic DNA using a subpopulation of a stool

sample, said method of determining “an” amount reads on claims drawn to determining “an” amount of patient genomic DNA in isolated cells from a stool sample comprising shed cells and shed cellular debris. The claims do not require one to determine the total amount of DNA in a stool sample from both the contained within intact exfoliated cells and substantially degraded DNA contained within shed cellular debris; rather, the claims are drawn to a method of determining “a” quantitative amount of genome equivalents of patient genomic DNA in a stool sample comprising shed cells and shed cellular debris, wherein the quantitative amount of genome equivalents is determined by measuring “an” amount of amplified nucleic acid fragments. The claims do not provide any limitation as to where or how said amplified nucleic acid fragments are to be obtained from the stool sample or any limitation requiring determining “the total” amount of DNA in a stool sample comprising shed cells and shed cellular debris. Further, motivation to express said amount in genome equivalents is discussed above.

In regards to the argument that Loktionov does not teach or suggest that detection of a 113 bp fragment was used to identify a patient as a candidate for additional testing, Loktionov et al teaches an amount of amplified 113 bp fragments of patient DNA in a stool sample is used to confirm DNA quality in order to identify a patient as a candidate for additional cancer testing if the amount is above a predetermined threshold amount, which would indicate a positive screen, before additional steps of diagnostic tests/examinations on the patient’s stool sample for detecting the presence of colorectal cancer are performed (see Figure 1 and page 338 , in particular).

The Examiner agrees that Hromadnikova does not teach or suggest a method of determining a quantitative amount of genome equivalents of patient genomic DNA in a stools sample comprising shed cells and cellular debris; however, said method is taught by the combined teachings of Loktionov et al and Hromadnikova for the reasons stated above.

In regards to the argument that that it was unexpected that measuring nucleic acid fragments of length 200bp or less could distinguish healthy patients from those that should undergo additional cancer testing and that said fragments having length of 200bp or less surprisingly provides an accurate measurement because it is indicative of the total amount of DNA that is present in a stool sample of both healthy individuals and cancer patients, Loktionov et al provides ample reasons why measuring nucleic acid fragments of length 200bp or less distinguishes patients that should undergo additional cancer testing such as Loktionov's 260/280 nm absorbance assay to detect the presence of colorectal cancer by detecting a quantitative amount of genomic DNA in a stool sample (see Table 2, Figure 2, and the paragraph spanning pages 340-340, in particular).

Claims 1, 4-8, 11, 14, 19-21, 24, 28-30, and 35-37 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Loktionov et al (Clinical Cancer Research, February 1998, 4(2): 337-342) in view of Hromadnikova et al (BMC Pregnancy and Childbirth, 5/28/02, 2(4):1-5) as applied to claims 1, 4, 7, 11, and 35 above, and further

in view of Ahlquist et al (Gastroenterology, 2000, 119:1219-1227), for the reasons stated in the Office Action of 4/28/08, and for the reasons set-forth below.

Anticipation of claims 1, 4, 7, 11, and 35 by the combined teachings of Loktionov et al and Hromadnikova et al is described above.

The combined teachings of Loktionov et al and Hromadnikova et al do not specifically teach methods of detecting the presence of abnormal proliferating colorectal cancer cells / detecting colorectal cancer / diagnosing colorectal cancer by: (1) performing a DNA integrity assay; (2) detecting a ras mutation, or (3) performing a colonoscopy. However, these deficiencies are rendered obvious or made up in the teachings of Ahlquist et al.

Ahlquist et al teaches methods for screening a patient for the presence of colon cancer comprising measuring a quantitative amount of genomic DNA in a stool sample, and identifying the patient as a candidate for additional disease testing or identifying patients with a positive screen if the amount of nucleic acid is above a predetermined threshold amount (pages 1221-1224, in particular). Ahlquist et al teaches colorectal cancer patients have higher fecal DNA yields than controls (page 1220 left column). Ahlquist et al further teaches methods of performing a DNA integrity assay (pages 1221-1222, in particular) and an assay to detect ras, p53, and BAT-26 mutations (page 12221 right column, in particular). Ahlquist et al further teaches colonoscopies as a means of detecting colon cancer (page 1219 right column, in particular). Ahlquist et al further teaches that fecal occult blood testing may detect cancers at an early stage; however, many cancers and most premalignant adenomas do not bleed and are missed

(page 1219 right column, in particular). Thus, Ahlquist et al indicate that the sensitive and specific markers they teach would improve the effectiveness and efficiency of stool screening prior to colonoscopy (page 1219 right column, in particular).

Further, one of ordinary skill in the art at the time the invention was made would have been motivated to perform the method of detecting the presence of abnormal proliferating colorectal cancer cells / detecting colorectal cancer / diagnosing colorectal cancer taught by the combined teachings of Loktionov et al and Hromadnikova et al (described above) and perform the additional steps of performing a DNA integrity assay, an assay to detect ras mutations, and a colonoscopy taught by Ahlquist et al because Loktionov et al teaches the need for performing numerous assays to detect colorectal cancer (see paragraph spanning pages 340-341, in particular) and the assays taught by Ahlquist et al aid in the detection of colorectal cancer. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for perform the method taught by the combined teachings of Loktionov et al and Hromadnikova et al with a DNA integrity assay, an assay to detect ras mutations, and a colonoscopy because Ahlquist et al teaches performing a DNA integrity assay (pages 1221-1222, in particular), an assay to detect ras mutations (page 12221 right column, in particular), and a colonoscopy (page 1219 right column, in particular). Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

In the Reply of 8/28/08, Applicant repeats arguments that have been addressed above.

New Rejections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4-8, 11, 14, 19-21, 24, 28-30, and 35-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lapidus et al (US 6,143,529; 11/7/00) in view of Hromadnikova et al (BMC Pregnancy and Childbirth, 5/28/02, 2(4):1-5).

Lapidus et al teaches a method for identifying a patient as a candidate for additional colorectal cancer testing comprising the steps of: determining a quantitative amount of patient genomic DNA in a stool sample comprising shed cells and shed cellular debris, wherein the quantitative amount is determined by using quantitative PCR to measure an amount of amplified nucleic acid fragments, wherein a high amount of amplifiable genomic DNA in a stool sample, as compared to a healthy individual, is highly predictive of colorectal cancer because patients with adenoma in the colon slough more cells than healthy individuals (see Example 2 and lines 42-46, in particular). Lapidus et al further teaches a quantitative amount of DNA in a sample would be obtained by detecting amplifiable nucleic acids less than 200bp in length (lines 43-47 of column 4, in particular). Lapidus et al further teaches that patients identified as

possibly having colon cancer by one method would also be subjected to other methods of testing for colon cancer (lines 8-10 of column 4, in particular). Such other methods comprise performing other diagnostic methods on the stool sample, LOH assay, detection of ras mutation, and colonoscopy (column 4, in particular).

Lapidus et al does not specifically teach a method wherein amounts of genomic DNA are expressed as "genome equivalents". However, this deficiency is made up in the teachings of Hromadnikova et al.

The teachings of Hromadnikova et al are discussed above.

One of ordinary skill in the art at the time the invention was made would have been motivated to perform the methods of Lapidus et al by expressing amounts of DNA in terms of genomic equivalents because expressing amounts of DNA in terms of genomic equivalents effectively normalizes data between multiple samples and assays. Further, one would have been motivated to perform said methods by detecting any amplifiable DNA, including amplified patient DNA having lengths of 200bp or less, wherein a patient is identified as a candidate for additional colorectal cancer testing if the amount of amplified patient genomic DNA having length of 200 bp or less is above a predetermined threshold level and wherein amounts of DNA are expressed as "genome equivalents" because Lapidus et al teaches a high amount of amplifiable genomic DNA in a stool sample, as compared to a healthy individual, is highly predictive of colorectal cancer because patients with adenoma in the colon slough more cells than healthy individuals (see Example 2 and lines 42-46, in particular). One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of

success for performing the methods of Lapidus et al by expressing amounts of DNA in terms of genomic equivalents and detecting amplified patient DNA having lengths of 200bp or less because Hromadnikova et al teaches how to determine genome equivalents and because Lapidus et al teaches a high amount of amplifiable genomic DNA in a stool sample, as compared to a healthy individual, is highly predictive of colorectal cancer because patients with adenoma in the colon slough more cells than healthy individuals (see Example 2 and lines 42-46, in particular). Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

Summary

No claim is allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SEAN E. AEDER whose telephone number is (571)272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sean E Aeder/
Examiner, Art Unit 1642